

Difference in Glucose Metabolism among Brain, Myocardium and Tumor

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III. 16 Difference in Glucose Metabolism among Brain, Myocardium and Tumor

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Introduction

Strong metabolic demand for glucose is apparently one of the common characteristics of brain, myocardium and tumor, but the correlation pattern with blood glucose is entirely different from one another. The present investigation was undertaken in order to make clear the difference of glucose demand among brain, myocardium and tumor.

Material and Methods

F-18 FDG was synthesized by method developed by Ido et al. Transplanted ascitic hepatoma (AH109A) cells were inoculated subcutaneously into male Donryu rats, weighing 100-150 g. When the tumor size reached about 1 cm diameter, rats were fasted for 0, 12, 24 and 36 hours prior to our experiments in order to obtain a wide range of blood glucose concentration. F-18 FDG was injected intravenously through a lateral tail vein of sixty rats. Thirty rats were treated with streptozotocin (40-80 mg/Kg) after overnight fasting, then F-18 FDG was injected 8 hour after streptozotocin (STZ) injection. They were killed by cervical dislocation at 10 min after F-18 FDG injection then blood, heart, brain and tumor were removed, bottled, weighed and counted in an automated NaI well counter. The radioactivity data were corrected for physical decay and expressed as percent injected dose per gram tissue (% dose/g tissue). Simultaneously, blood glucose concentrations were measured by standard enzymatic methods. The same experiment was done with sixty normal rats.

Results

We investigated the correlation between F-18 FDG uptake and blood glucose concentration in this study. There was little difference between normal and tumor-bearing rat in uptakes of F-18 FDG by brain and myocardium of tumor-bearing rats with those of normal rats. The data of the brain uptake were showed in Fig. 1. The uptake of the brain decreased with increasing blood glucose linearly. Of the great interest was strong negative correlation of the brain uptake with blood glucose. The correlation coefficient was -0.86 and the equation of regression line was $y = -0.018x + 4.8$. But myocardial uptake was entirely different from that of brain. The correlation between myocardial uptake and blood glucose were presented in Fig. 2. Myocardial uptake of F-18 FDG was almost unchanged under about 120 mg % of blood glucose, then increased

steeply with increasing blood glucose. On the other hand, tumor uptake pattern remained relatively unchanged, irrespective of blood glucose. These results were showed in Fig. 3. We divided brain and myocardial uptake into blood glucose groups of 10 mg %. Tumor uptakes were divided into blood glucose groups of 20 mg % because number of the data was not sufficient. They were presented in Fig. 4. It was obvious that glucose metabolism is entirely different among brain, heart and tumor. Effects of STZ on F-18 FDG uptakes of brain, heart and tumor were showed in Fig. 5. When STZ induced hyperglycemia (above 200 mg % of blood glucose), uptake patterns were similar to one another. Brain and myocardial uptakes decreased but tumor uptake remained relatively unchanged.

Discussion

Because glucose is the major energy source of brain, many attempts have been made to utilize nonphysiological glucose analog, F-18 FDG to measure the local cerebral metabolic rate of glucose. Glucose is an important physiological substrate for myocardium also, therefore F-18 FDG was utilized to estimate the myocardial metabolic rate of glucose. Moreover, increased glycolysis in cancer cells has been well documented by many investigators and various attempts have been made to use nonphysiological glucose analogs including FDG for cancer therapy and detection. But we clarified that the correlation patterns between F-18 FDG uptake and blood glucose were entirely different from one another. It was presumed that the antagonists of glucose might interfere with the formation of the glycosidic ring of deoxyribonucleic acid (DNA) and might impede the multiplication of malignant cells by inhibiting their glycosis. W-Deoxy-D-glucose (2DG) is an analog of glucose and was studied about antitumor effect by many investigators. But these attempts did not succeed because of toxic effects, such as coma, convulsion, ataxia and edema. These results may be expected from our present data with F-18 FDG. Brain and myocardium were markedly dependent upon glucose metabolism. Therefore, if brain and myocardial uptake of 2DG are suppressed and tumor uptake remains unchanged, toxic effects may be diminished and antitumor effect will be augmented. According our present results, there is an possibility that this condition may be accomplished by STZ treatment.

References

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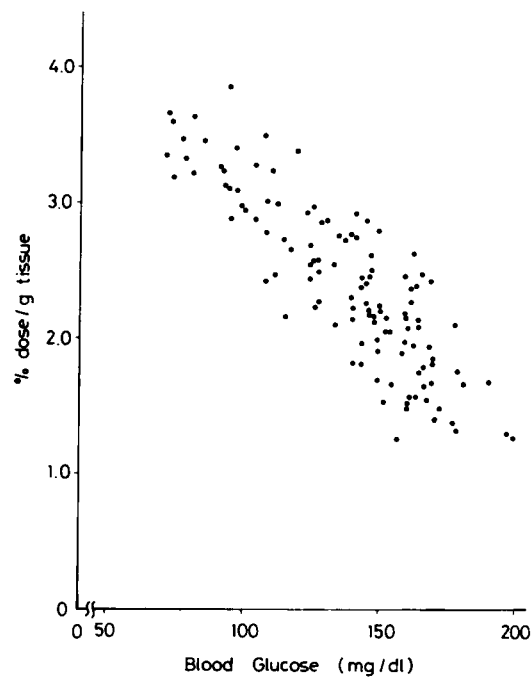


Fig. 1. Correlation between brain uptake of F-18 FDG and blood glucose the uptake of the brain decreased with increasing blood glucose linearly. The correlation coefficient was -0.86 and the equation of regression line was $y = -0.018x + 4.8$.

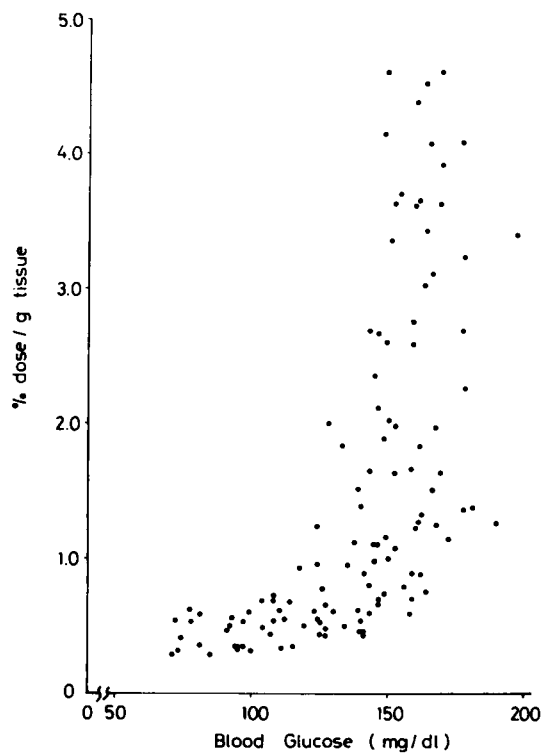


Fig. 2. Correlation between myocardial uptake of F-18 FDG and blood glucose myocardial uptake was almost unchanged under about 120 mg % of blood glucose, then increased steeply with increasing blood glucose.

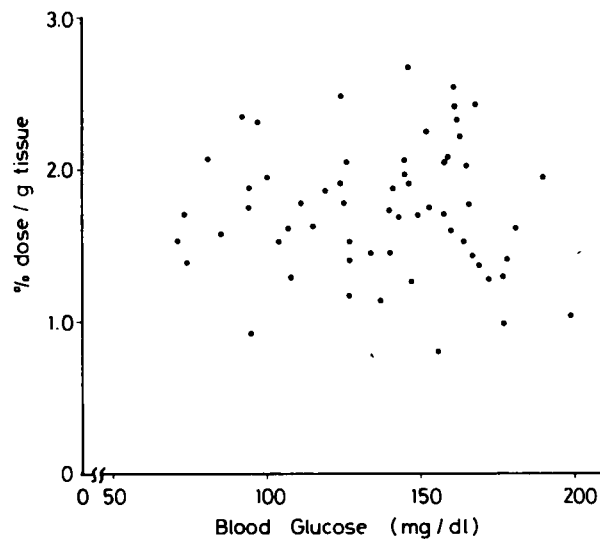


Fig. 3. Correlation between tumor uptake of F-18 FDG and blood glucose. Tumor uptake remained relatively unchanged, irrespective of blood glucose.

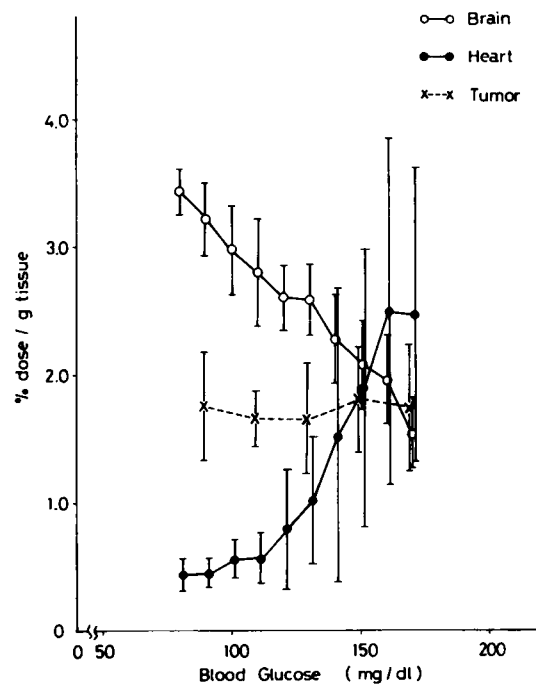


Fig. 4. Correlation between F-18 FDG uptake and blood glucose. \circ — \circ : brain
 \bullet — \bullet : myocardium \times — \times : tumor Each point represents the Mean \pm SD.

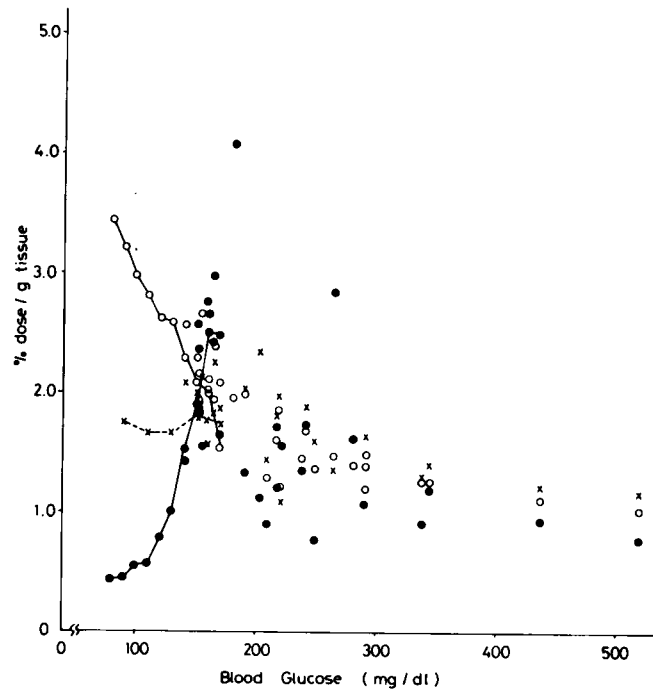


Fig. 5. Effects of STZ on F-18 FDG uptakes of brain, myocardium and tumor.
 o: brain ●: myocardium x: tumor When STZ induced hyper-
 glycemia (above 200 mg % of blood glucose) uptake patterns were similar
 to one another.